REMARKS

Reconsideration and withdrawal of the rejections of the application are requested in view of these amendments and remarks, which place the application into condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1, 2, 8, 18, 29-33, 35, and 36 are pending in this application. Claims 1, 8, and 35 are amended; claim 36 is added and reads upon the elected embodiments; and claims 19-24 and 34 are cancelled. Support for the amendment to claim 1 can be found on page 5, line 33 – page 6, line 28 as originally filed, and in cancelled claim 34. Support for the amendment to claim 8 can be found on page 9, lines 19-28 as originally filed. Support for new claim 36 can be found on page 48, line 26 – page 50, line 49 as originally filed, on page 38, lines 25-30 as amended on June 28, 2004, and in Figures 9-11. No new matter is added.

It is submitted that the claims are patentably distinct over the prior art and that these claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but simply for clarification and to round out the scope of protection to which Applicants are entitled.

Claim Objections

Claim 8 was objected to for reciting "ligand" in its plural form, which is inconsistent with the singular form recited in claim 1. Claim 8 is amended to recite "ligand" in its singular form.

II. THE REJECTIONS UNDER 35 U.S.C. § 112 ARE OVERCOME

Enablement

Claims 1, 2, 8, 18-24, 29, 31, 34, and 35 were rejected under the first paragraph of Section 112 as allegedly lacking enablement. The rejection is traversed.

The instant invention is directed to a conjugate comprising (i) a sequence comprising an antibody or antibody fragment which binds to an APC and (ii) a sequence comprising a Notch DSL domain and at least one EGF-like repeat. Consequently, in contrast to the allegation on page 8 of the Office Action, the scope of the instant invention does not encompass a first sequence that can be a ligand, receptor, or superantigen from any bacteria or any virus. One of skill in the art would know how to obtain antibodies or antibody fragments against a predetermined antigen, as such methods are well known in the art. The present specification

provides sufficient guidance on page 13, lines 12-21 for assays which identify molecules, *i.e.,* fragments, which bind to APC surface molecules. Such assays are well within the ordinary skill of the artisan and do not constitute undue experimentation.

In addition, Applicants disagree with the Office Action's allegation that the specification is enabling only for a second sequence comprising the Notch ligands human Delta 1, Delta 3, Delta 4, Jagged 1, and Jagged 2. The second sequence of the instant invention is directed to a Notch ligand DSL domain and at least one EGF-like repeat, and there is sufficient guidance in the specification and figures, and knowledge in the field at the time the application was filed, to enable the invention as claimed. For example, the specification discloses that Notch ligands display multiple EGF-like repeats and a DSL domain (page 43, lines 20-31, and Figures 2 and 3), and lists examples of mammalian Notch ligands identified at the time the application was filed (page 9, lines 19-28). Knowledge in the field at the time of filing also confirms the specification's disclosure that Notch ligands display multiple EGF-like repeats and a DSL domain (Artavantis-Tsakonas, *et al.* Science 284: 770-776, 1999).

The specification further notes that "homology between [Notch ligand] family members is extensive" (page 9, line 27), which thereby suggests that one skilled in the art can apply the guidance provided by the specification to easily obtain the Notch ligands encompassed by the scope of the instant claims. Applicants' arguments are further supported by Figure 8, which shows schematic representations of the Notch ligands Jagged and Delta and confirms the presence of a DSL domain and at least one EGF-like repeat in these ligands, and Figure 9, which shows aligned amino acid sequences of DSL domains from various Drosophila and mammalian Notch ligands and confirms that a DSL domain and at least one EGF-like repeat is widely present. Therefore, based on the teachings of the specification and figures, and in consideration of what was known in the art at the time the present application was filed, one skilled in the art would not require undue experimentation to obtain a sequence comprising a Notch ligand DSL domain and at least one EGF-like repeat while retaining Notch signalling activity.

Applicants additionally note that the term "superantigen" is no longer recited in the claims. Therefore, any rejection based on such language is moot.

Also, new claim 36 recites the Notch ligand sequences, which the Office Action concedes is enabled by the specification (page 8).

Written Description

Claims 1, 2, 8, 18-24, 29, 31, 34, and 35 were rejected under the first paragraph of Section 112 as allegedly lacking adequate written description. The rejection is traversed.

As discussed above, the first sequence of the instant invention is directed to antibody or antibody fragments, which are amply described in the specification, for example, at page 5, line 33 – page 6, line 28. Further, at page 13, lines 5-21, the specification describes the APC molecules to which the antibodies bind, *e.g.*, CD205 (DEC205), CD204, CD14, CD206, TLRs, Langerin (CD207), DC-SIGN (CD209), CD32, CD68, CD83, CD33, CD54 or BDCA-2,3,4, which provides additional description of the structure of the antibody. Thus, contrary to the Office Action's assertions, the structure of the first sequence of the invention is sufficiently described in the specification.

In addition, Applicants reiterate that the second sequence of the invention, comprising a Notch ligand DSL domain and at least one EGF-like repeat, is sufficiently described in the specification and Figures. As noted above, the specification discusses that Notch ligands display multiple EGF-like repeats and a DSL domain (page 43, lines 20-31), and lists examples of mammalian Notch ligands, among which there is extensive homology (page 9, lines 19-28). Furthermore, Figures 2 and 3 show schematic representations of Notch and the Notch intracellular domain, Figure 8 shows schematic representations of the Notch ligands Jagged and Delta, and Figure 9 shows aligned amino acid sequences of DSL domains from various Drosophila and mammalian Notch ligands. Thus, there is indeed ample description of the structure of the claimed Notch ligands.

The other issues raised by the Examiner regarding written description have been cured by the amendments to the claims.

Applicants further note that new claim 36 recites the Notch ligand sequences, which the Office Action concedes is sufficiently described by the specification (page 12).

Indefiniteness

Claims 2 and 9 were rejected under the second paragraph of Section 112 as allegedly being indefinite. The rejection is traversed.

The Office Action admits that transforming host cell produces fusion protein, but alleges that a conjugate is not produced by this method. Applicants disagree and draw attention to the specification which recites "conjugates include fusion proteins in which the targeting protein is

linked to a protein for T cell signalling modulation" (see page 4, lines 4-17). Therefore, the conjugate of the claimed invention can be a fusion protein and can be prepared by transforming a cell.

Accordingly, reconsideration and withdrawal of all Section 112 rejections are requested.

III. THE REJECTION UNDER 35 U.S.C. § 102 IS OVERCOME

Claims 1, 2, 8, 29, 31, 34, and 35 were rejected under Section 102(b) as allegedly being anticipated by WO 98/20142. In WO 98/20142 there is no specific and unambiguous disclosure of a conjugate comprising a first sequence comprising an antibody or fragment thereof which binds to an APC. Thus, the present invention is distinguished over WO 98/20142.

Reconsideration and withdrawal of the Section 102 rejection is requested.

IV. THE REJECTIONS UNDER 35 U.S.C. § 103 ARE OVERCOME

Claims 1 and 18-24 were rejected under Section 103(a) as allegedly being unpatentable over WO 98/20142 in view of WO 98/26747. However, as discussed above, WO 98/20142 does not specifically and unambiguously teach or suggest a conjugate comprising a first sequence comprising an antibody or fragment thereof which binds to an APC. Furthermore, WO 98/26747 is directed to the situation where the second sequence is a tumor specific antigen, such as MAGE-1, MAGE-3 and MART-1. Thus, WO98/26747 does not teach a skilled worker anything about the present invention. Both the first and second sequences are different to those now claimed.

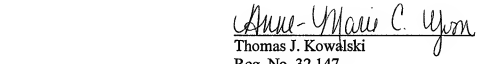
Accordingly, reconsideration and withdrawal of the Section 103 rejection is requested.

CONCLUSION

This application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants



Thomas J. Kowalski
Reg. No. 32,147

Anne-Marie C. Yvon, Ph.D.
Reg. No. 52,390
(212) 588-0800